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=> dup rem l3
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L4 131 DUP REM L3 (32 DUPLICATES REMOVED)

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L5 80 L4 AND PY<=2003

=> s l5 and (brain or heart or liver or kidney or gastro intestinal tract or spleen or muscle or eye or ganglion or lung or gonad or pancreas)
L6 24 L5 AND (BRAIN OR HEART OR LIVER OR KIDNEY OR GASTRO INTESTINAL
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L6 ANSWER 1 OF 24 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN
AN 2003449944 EMBASE
TI Adipose-derived adult stem cells: Isolation, characterization, and differentiation potential.
AU Gimble J.M.; Guilak F.
CS J.M. Gimble, Pennington Biomedical Research Ctr., Louisiana State University, 6400 Perkins Rd., Baton Rouge, LA 70808, United States
SO Cytotherapy, (2003) Vol. 5, No. 5, pp. 362-369. .
Refs: 67
ISSN: 1465-3249 CODEN: CYTRF3
CY United Kingdom
DT Journal; General Review
FS 029 Clinical Biochemistry
027 Biophysics, Bioengineering and Medical Instrumentation
030 Pharmacology
036 Health Policy, Economics and Management
037 Drug Literature Index
LA English
SL English
ED Entered STN: 20 Nov 2003
Last Updated on STN: 20 Nov 2003
AB Adipose tissue is an abundant, accessible, and replenishable source of adult stem cells that can be isolated from liposuction waste tissue by collagenase digestion and differential centrifugation. These adipose-derived adult stem (ADAS) cells are multipotent, differentiating along the adipocyte, ***chondrocyte*** , myocyte, neuronal, and osteoblast lineages, and can serve in other capacities, such as providing hematopoietic support and gene transfer. ADAS cells have potential applications for the repair and regeneration of acute and chronically damaged tissues. Additional pre-clinical safety and efficacy studies will be needed before the promise of these cells can be fully realized.

L6 ANSWER 2 OF 24 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN
AN 2002390316 EMBASE
TI Primary human cells differ in their susceptibility to rAAV-2-mediated gene transfer and duration of reporter gene expression.
AU Rohr U.-P.; Kronenwett R.; Grimm D.; Kleinschmidt J.; Haas R.
CS U.-P. Rohr, Klin. Hamat., Onkol./Klin. Immunol., Heinrich-Heine-Univ. Dusseldorf, Moorenstrasse 5, D-40225 Dusseldorf, Germany. urohr-uni-duesseldorf@gmx.de
SO Journal of Virological Methods, (2002) Vol. 105, No. 2, pp. 265-275. .
Refs: 33
ISSN: 0166-0934 CODEN: JVMEDH
PUI S 0166-0934(02)00117-9
CY Netherlands
DT Journal; Article
FS 004 Microbiology
LA English
SL English
ED Entered STN: 21 Nov 2002
Last Updated on STN: 21 Nov 2002
AB The susceptibility of a variety of different primary tissues was examined to long-term transduction with recombinant adeno-associated virus type 2 (rAAV-2) and factors influencing the transduction efficiency. In contrast to others using cell lines and animal models, emphasis was placed on the use of primary human cells. Enhanced green fluorescent protein (EGFP) marker gene expression was examined using fluorescence-activated cell sorting analysis. The most effective target cells for rAAV-2-mediated gene transfer were bronchial epithelial, artery endothelial as well as smooth and skeletal ***muscle*** cells with mean transduction rates ranging from 34.3 to 81.6%. Lower transduction rates between 4.3 and 19.5% were found in ***chondrocytes*** , dermal papilla follicle epithelial cells and fibroblasts. No transduction was observed in melanocytes, granulocyte colony-stimulating factor (G-CSF)-mobilized CD34(+) cells or malignant CD19(+) cells from patients with chronic lymphocytic leukemia. A proportion of EGFP-expressing skeletal ***muscle*** and smooth ***muscle*** cells was maintained over a period of 6 weeks after transduction (42.7.+-.5.4 and 67.1.+-.0.9%,

respectively). Interestingly, among hair follicle epithelial cells the proportion of transduced cells increased from 8.+-.0.5 to 36.+-.7.7% in the course of 6 weeks. In contrast, for endothelial cells, bronchial epithelial cells and fibroblasts, a rapid decline in the number of EGFP expressing cells were noted. An inverse relationship between the proportion of cells in G2/M phase of cell cycle and long-term gene expression was observed. All rAAV-2 susceptible primary cells expressed FGFR-1 and the .alpha.V integrin consistent with their role as co-receptors for AAV-2. In conclusion, AAV-2 is a suitable ***vector*** system for transduction and evaluation of functional effects of long-term gene expression in primary human ***muscle*** and hair follicle cells. .COPYRGT. 2002 Elsevier Science B.V. All rights reserved.

L6 ANSWER 3 OF 24 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN
AN 1999310161 EMBASE
TI In vivo endochondral bone formation using a bone morphogenetic protein 2 adenoviral ***vector*** .
AU Alden T.D.; Pittman D.D.; Hankins G.R.; Beres E.J.; Engh J.A.; Das S.; Hudson S.B.; Kerns K.M.; Kallmes D.F.; Helm G.A.
CS Dr. G.A. Helm, Department of Neurosurgery, Health Sciences Center, University of Virginia, Charlottesville, VA 22908, United States. gah9r@virginia.edu
SO Human Gene Therapy, (1 Sep 1999) Vol. 10, No. 13, pp. 2245-2253. .
Refs: 51
ISSN: 1043-0342 CODEN: HGTHE3
CY United States
DT Journal; Article
FS 022 Human Genetics
031 Arthritis and Rheumatism
033 Orthopedic Surgery
LA English
SL English
ED Entered STN: 16 Sep 1999
Last Updated on STN: 16 Sep 1999
AB Bone morphogenetic proteins (BMPs) are polypeptides that induce ectopic bone formation in standard rat in vivo assay systems. Previous studies have demonstrated the clinical utility of these proteins in spinal fusion, fracture healing, and prosthetic joint stabilization. Gene therapy is also a theoretically attractive technique to express BMPs clinically, since long- term, regulatable gene expression and systemic delivery with tissue-specific expression may be possible in future. This study was performed to determine whether an adenoviral ***vector*** containing the BMP-2 gene can be used to express BMP-2 in vitro and promote endochondral bone formation in vivo. In vitro, U87 MG Cells transduced per cell with 20 MOI of an adenoviral construct containing the BMP-2 gene under the control of the universal CMV promoter (Ad-BMP-2) showed positive antibody staining for the BMP-2 protein at posttransfection day 2. The synthesis and secretion of active BMP-2 into the conditioned medium of Ad-BMP-2-transduced 293 cells were confirmed by Western blot analysis and the induction of alkaline phosphatase activity in a W-20 stromal cell assay. In vivo, Sprague-Dawley rats and athymic nude rats were injected with Ad-BMP-2 in the thigh musculature and were sacrificed on day 3, 6, 9, 12, 16, 21, 60, and 110 for histological analysis. The Sprague-Dawley rats showed evidence of acute inflammation, without ectopic bone formation, at the injection sites. In the athymic nude rats, BMP-2 gene therapy induced mesenchymal stem cell chemotaxis and proliferation, with subsequent differentiation to ***chondrocytes*** . The ***chondrocytes*** secreted a cartilaginous matrix, which then mineralized and was replaced by mature bone. This study demonstrates that a BMP-2 adenoviral ***vector*** can be utilized to produce BMP-2 by striated ***muscle*** cells in athymic nude rats, leading to endochondral bone formation. However, in immunocompetent animals the endochondral response is attenuated, secondary to the massive immune response elicited by the first- generation adenoviral construct.

L6 ANSWER 4 OF 24 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN
AN 1998201962 EMBASE
TI Overexpression of transforming growth factor .beta.1 in arterial endothelium causes hyperplasia, apoptosis, and cartilaginous metaplasia.
AU Schulick A.H.; Taylor A.J.; Zuo W.; Qiu C.-B.; Dong G.; Woodward R.N.; Agah R.; Roberts A.B.; Virmani R.; Dichek D.A.
CS D.A. Dichek, Gladstone Inst. of Cardiovasc. Dis., P.O. Box 419100, San Francisco, CA 94141-9100, United States
SO Proceedings of the National Academy of Sciences of the United States of America, (9 Jun 1998) Vol. 95, No. 12, pp. 6983-6988. .
Refs: 46
ISSN: 0027-8424 CODEN: PNASA6
CY United States
DT Journal; Article
FS 005 General Pathology and Pathological Anatomy
018 Cardiovascular Diseases and Cardiovascular Surgery
029 Clinical Biochemistry
LA English
SL English
ED Entered STN: 14 Aug 1998
Last Updated on STN: 14 Aug 1998
AB Uninjured rat arteries transduced with an adenoviral ***vector*** expressing an active form of transforming growth factor .beta.1 (TGF-.beta.1) developed a cellular and matrix-rich neointima, with cartilaginous metaplasia of the vascular media. Explant cultures of transduced arteries showed that secretion of active TGF-.beta.1 ceased by 4 weeks, the time of maximal intimal thickening. Between 4 and 8 weeks, the cartilaginous metaplasia resolved and the intimal lesions regressed almost completely, in large part because of massive apoptosis. Thus, locally expressed TGF-.beta.1 promotes intimal growth and appears to cause transdifferentiation of vascular smooth ***muscle*** cells into ***chondrocytes*** . Moreover, TGF-.beta.1 withdrawal is associated with regression of vascular lesions. These data suggest an unexpected plasticity of the adult vascular smooth ***muscle*** cell phenotype and provide an etiology for cartilaginous metaplasia of the arterial wall. Our observations may help to reconcile divergent views of the role of TGF-.beta.1 in vascular ***disease*** .

L6 ANSWER 5 OF 24 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
AN 2002:535941 BIOSIS
DN PREV200200535941
TI ***Muscle*** derived, cell based ex vivo gene therapy for treatment of full thickness articular cartilage defects.
AU Adachi, Nobuo; Sato, Kenji; Usas, Arvydas; Fu, Freddie H.; Ochi, Mitsuo; Han, Chang-Whan; Niyibizi, Christopher; Huard, Johnny [Reprint author]
CS Growth and Development Laboratory, Children's Hospital of Pittsburgh, 3705 Fifth Avenue, 4151 Rangos Research Center, Pittsburgh, PA, 15213, USA jhuard+@pitt.edu
SO Journal of Rheumatology, (***September, 2002***) Vol. 29, No. 9, pp. 1920-1930. print.
CODEN: JRHUA9. ISSN: 0315-162X.
DT Article
LA English
ED Entered STN: 16 Oct 2002
Last Updated on STN: 16 Oct 2002
AB Objective. To evaluate the effectiveness of transplanted allogeneic ***muscle*** derived cells (MDC) embedded in collagen gels for the treatment of full thickness articular cartilage defects, to compare the results to those from ***chondrocyte*** transplantation, and to evaluate the feasibility of MDC based ex vivo gene therapy for cartilage repair. Methods. Rabbit MDC and ***chondrocytes*** were transduced with a retrovirus encoding for the beta-galactosidase gene (LacZ). The cells were embedded in type I collagen gels, and the cell proliferation and transgene expression were investigated in vitro. In vivo, collagen gels containing transduced cells were grafted to the experimental full thickness osteochondral defects. The repaired tissues were evaluated histologically and histochemically, and collagen typing of the tissue was performed. Results. The MDC and ***chondrocyte*** cell numbers at 4 weeks of culture were 305 +- 25% and 199 +- 25% of the initial cell number, respectively. The initial percentages of LacZ positive cells in the MDC and ***chondrocyte*** groups were 95.4 +- 1.9% and 93.4 +- 3.4%, and after 4 weeks of culture they were 84.2 +- 3.9% and 76.9 +- 4.3%, respectively. In vivo, although grafted cells were found in the defects only up to 4 weeks after transplantation, the repaired tissues in the MDC and ***chondrocyte*** groups were similarly better histologically than control groups. Repaired tissues in the MDC group were mainly composed of type II collagen, as in the ***chondrocyte*** group. Conclusion. Allogeneic MDC could be used for full thickness articular cartilage repair as both a gene delivery vehicle and a cell source for tissue repair.

L6 ANSWER 6 OF 24 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
AN 2002:460907 BIOSIS
DN PREV200200460907
TI SOX9 interacts with a component of the human thyroid hormone receptor-associated protein complex.
AU Zhou, Rongjia; Bonneaud, Nathalie; Yuan, Chao-Xing; De Santa Barbara, Pascal; Boizet, Brigitte; Tibor, Schomber; Scherer, Gerd; Roeder, Robert G.; Poulat, Francis; Berta, Philippe [Reprint author]
CS Human Molecular Genetics Group, Institut de Genetique Humaine, UPR1142 CNRS, 141 rue de la Cardonille, 34396, Montpellier Cedex, 5, France berta@igh.cnrs.fr
SO Nucleic Acids Research, (***July 15, 2002***) Vol. 30, No. 14, pp. 3245-3252. print.
CODEN: NARHAD. ISSN: 0305-1048.
DT Article
LA English
ED Entered STN: 28 Aug 2002
Last Updated on STN: 28 Aug 2002
AB SOX9 transcription factor is involved in ***chondrocyte*** differentiation and male sex determination. Heterozygous defects in the human SOX9 gene cause campomelic dysplasia. The mechanisms behind SOX9
function are not understood despite the description of different target genes. This study therefore sets out to identify SOX9-associated proteins to unravel how SOX9 interacts with the cellular transcription machinery. We report the ability of SOX9 to interact with TRAP230, a component of the thyroid hormone receptor-associated protein (TRAP) complex. Both in vitro and in vivo assays have confirmed that the detected interaction is specific and occurs endogenously in cells. Using co-transfection experiments, we have also shown that the TRAP230 interacting domain can act in a dominant-negative manner regarding SOX9 activity. Our results add SOX9 to the list of activators that communicate with the general transcription machinery through the TRAP complex and suggest a basis for the collaboration of SOX9 with different coactivators that could contact the same coactivator/integrator complex.

L6 ANSWER 7 OF 24 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
AN 2002:172183 BIOSIS
DN PREV200200172183
TI Gene therapy for rheumatoid arthritis: Lessons from animal models, including studies on interleukin-4, interleukin-10, and interleukin-1 receptor antagonist as potential ***disease*** modulators.
AU van de Loo, Fons A.J. [Reprint author]; van den Berg, Wim B.
CS Department of Rheumatology, University Medical Center Nijmegen, Geert Grooteplein 26-28, 6500 HB, Nijmegen, Netherlands
a.vandeloo@reuma.azn.nl
SO Rheumatic Disease Clinics of North America, (***February, 2002***) Vol. 28, No. 1, pp. 127-149. print.
ISSN: 0889-857X.
DT Article
General Review; (Literature Review)
LA English
ED Entered STN: 5 Mar 2002
Last Updated on STN: 5 Mar 2002

L6 ANSWER 8 OF 24 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
AN 2002:163473 BIOSIS
DN PREV200200163473
TI In utero transduction of ***lung*** and ***liver*** : Gestational age determines gene transfer efficiency.
AU Porada, Christopher D. [Reprint author]; Almeida-Porada, M. Graca [Reprint author]; Park, Paul [Reprint author]; Zanjani, Esmail D. [Reprint author]
CS Dept. of Medicine, VAMC, University of Nevada, Reno, NV, USA
SO Blood, (***November 16, 2001***) Vol. 98, No. 11 Part 1, pp. 215a. print.
Meeting Info.: 43rd Annual Meeting of the American Society of Hematology, Part 1. Orlando, Florida, USA. December 07-11, 2001. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LA English
ED Entered STN: 5 Mar 2002
Last Updated on STN: 5 Mar 2002
AB We have previously demonstrated that the direct injection of retroviral vectors into pre-immune fetal sheep results not only in the successful transduction of long-term engrafting hematopoietic stem cells, but also in the widespread distribution of ***vector*** to all other tissues examined (Human Gene Therapy 9:1571, 1998 and Blood 11:3417, 2001). In the present study, we performed a detailed analysis of the ***liver*** and lungs of animals receiving murine retroviral ***vector*** supernatants in utero to determine whether non-hematopoietic cells within these tissues were transduced and also examined whether the time of administration of ***vector*** during the period of pre-immunity (54 days, 57 days, and 65 days; term: 145 days) would impact upon the levels of gene transfer to the non-hematopoietic cells within these tissues. Our analysis of the ***liver*** of these sheep revealed foci each consisting of 18-30 transduced hepatocytes, representing 2-3% of the total hepatocytes present within the ***liver*** sections. Hepatic transgene expression was not limited to hepatocytes, but was also present within the endothelium of hepatic blood vessels. When comparing the ***liver*** sections from animals that had received the ***vector*** at different gestational ages, we observed an inverse correlation between recipient age and the efficiency of gene transfer to the hepatocytes, such that a high efficiency of gene transfer occurred at 54 days, a moderate level occurred at 57 days, and very little (10-fold less) occurred at 65 days of gestation. Interestingly, analysis of the lungs of these same animals revealed that the efficiency of transduction of non-hematopoietic ***lung*** tissue increased with increasing gestational age. Within the ***lung*** , the majority of transgene expressing cells were epithelial cells and fibroblasts of the interalveolar septi. Alveolar macrophages and airway ***chondrocytes*** within the forming hyaline cartilage were transduced at low levels. These results demonstrate that multiple non-hematopoietic cells types within the ***liver*** and ***lung*** are transduced following direct injection of murine retroviral ***vector*** supernatants into the peritoneal cavity of pre-immune fetal sheep and suggest that the developmental stage of each organ at the time of injection may determine its susceptibility to in utero gene transfer. The presence/expression of the transgene within multiple cell types in these organs suggests that this approach may be useful in the treatment of diseases such as cystic fibrosis and hemophilia that produce pathology within the ***lung*** and ***liver*** , respectively, early in development. In addition, the successful transduction of ***liver*** endothelial cells may help to explain the induction of long-term immune tolerance to transgene products that we have thus far observed in animals receiving in utero gene transfer (Blood 11:3417, 2001).

L6 ANSWER 9 OF 24 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
AN 2001:473327 BIOSIS
DN PREV200100473327
TI A polymorphism of the human matrix gamma-carboxyglutamic acid protein promoter alters binding of an activating protein-1 complex and is associated with altered transcription and serum levels.
AU Farzaneh-Far, Afshin [Reprint author]; Davies, John D.; Braam, Levienja A.; Spronk, Henri M.; Proudfoot, Diane; Chan, Shiu-Wan; O'Shaughnessy, Kevin M.; Weissberg, Peter L.; Vermeer, Cees; Shanahan, Catherine M.
CS Division of Cardiovascular Medicine, University of Cambridge, Addenbrooke's Hospital, Hills Road, ACCI Level 6, Cambridge, CB22QQ, UK
aff24@cam.ac.uk
SO Journal of Biological Chemistry, (***August 31, 2001***) Vol. 276, No. 35, pp. 32466-32473. print.
CODEN: JBCHA3. ISSN: 0021-9258.
DT Article
LA English
ED Entered STN: 10 Oct 2001
Last Updated on STN: 23 Feb 2002
AB Matrix gamma-carboxyglutamic acid protein (MGP) is a mineral-binding extracellular matrix protein synthesized by vascular smooth ***muscle*** cells (VSMCs) and ***chondrocytes*** that is thought to be a key regulator of tissue calcification. In this study, we identified four polymorphisms in the promoter region of the human MGP gene. Transfection studies showed that the G-7A and T-138C polymorphisms have an important impact on in vitro promoter activity when transiently transfected into VSMCs. We found that one of these polymorphisms (T-138C) is significantly correlated with serum MGP levels in human subjects. Promoter deletion analysis showed that this polymorphism lies in a region of the promoter critical for transcription in VSMCs. This region contains a potential activating protein-1 (AP-1) binding element located between -142 and -136. We have demonstrated that the T-138C polymorphism results in altered binding of an AP-1 complex to this region. The -138T allelic variant binds AP-1 complexes consisting primarily of c-Jun, JunB and its partners Fra-1 and Fra-2 in rat VSMC. Furthermore, the -138T variant form of the promoter was induced following phorbol 12-myristate 13-acetate treatment, while the -138C variant was refractive to phorbol 12-myristate 13-acetate treatment, confirming that AP-1 factors preferentially bind to the -138T variant. This study therefore suggests that a common polymorphism of the MGP promoter influences binding of the AP-1 complex, which may lead to altered transcription and serum levels. This could have important implications for diseases such as atherosclerosis and aortic valve stenosis, since it strongly suggests a genetic basis for regulation of tissue calcification.

L6 ANSWER 10 OF 24 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
AN 1999:428748 BIOSIS
DN PREV199900428748
TI Direct adenovirus-mediated gene delivery to the temporomandibular joint in guinea-pigs.
AU Kuboki, Takuo; Nakanishi, Tohru; Kanyama, Manabu; Sonoyama, Wataru; Fujisawa, Takuo; Kobayashi, Kappei; Ikeda, Takumi; Kubo, Toshikazu; Yamashita, Atsushi; Takigawa, Masaharu [Reprint author]
CS Department of Biochemistry and Molecular Dentistry, Okayama University Dental School, Okayama, Japan
SO Archives of Oral Biology, (***Sept., 1999***) Vol. 44, No. 9, pp. 701-709. print.
CODEN: AOBIAR. ISSN: 0003-9969.
DT Article
LA English
ED Entered STN: 18 Oct 1999
Last Updated on STN: 18 Oct 1999
AB Adenovirus ***vector*** system is expected to be useful for direct gene therapy for joint ***disease*** . This study first sought to confirm that foreign genes can be transferred to articular ***chondrocytes*** in primary culture. Next, recombinant adenovirus vectors harbouring beta-galactosidase gene (LacZ) was injected directly into the temporomandibular joints of Hartley guinea-pigs to clarify the in vivo transfer availability of the adenovirus vectors. Specifically, recombinant adenovirus harbouring LacZ gene (Ax1CALacZ) was injected into the upper joint cavities of both mandibular joints of four male 6-week-old Hartley guinea-pigs. Either the same amount of recombinant adenovirus without LacZ gene (Ax1w) suspension (placebo) or the same amount of phosphate-buffered saline solution (control) were injected into the upper joint cavities of both joints of another four male guinea-pigs. At 1, 2, 3 and 4 weeks after injection, the joints were dissected and the expression of delivered LacZ was examined by 5-bromo-4-chloro-3-indolyl-beta-D-galactopyranoside (X-gal) staining and reverse transcriptase-polymerase chain reaction (RT-PCR). To investigate the expression of transferred gene in other organs, total RNA was extracted from ***liver*** , ***kidney*** , ***heart*** and ***brain*** and the expression of LacZ mRNA and 18 S ribosomal RNA were analysed by RT-PCR. Clear expression of LacZ was observed in the articular surfaces of the temporal tubercle, articular disc and synovium of the temporomandibular joints even 4 weeks after injection in the Ax1CALacZ-injected group, while no expression was detected in placebo and control groups. Histological examination confirmed that LacZ activity was clearly detected in a few cell layers of the articular surface tissues, which is much more efficient than in a previously study of the knee joint. In the other organs, expression of the delivered transgene was not observed. Based on these findings, direct gene delivery into the articular surface of the temporomandibular joint using the adenovirus ***vector*** is feasible as an effective in vivo method.

L6 ANSWER 11 OF 24 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:802547 CAPLUS
DN 141:290057
TI Gene therapy vectors expressing both isoforms of .beta.-hexosaminidase
IN Kyrkanides, Stephanos

PA USA
SO U.S. Pat. Appl. Publ., 169 pp., Cont.-in-part of Appl. No. PCT/US03/13672.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2004192630	A1	20040930	US 2004-781142	20040218
WO 2003092612	A2	20031113	WO 2003-US13672	20030502 <--
WO 2003092612	A3	20041104		

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WO 2005080409	A1	20050901	WO 2005-US4885	20050216

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2002-377503P P 20020502
WO 2003-US13672 A2 20030502
US 2004-781142 A 20040218

AB Disclosed are compns. and methods related to nucleic acid constructs contg. a .beta.-hexosaminidase .beta. (HexB)-encoding element and a .beta.-hexosaminidase .alpha. (HexA)-encoding element. In one such ***vector*** using feline immunodeficiency virus, the cytomegalovirus promoter drives transgene expression, and the translation of the second open reading frame, HexB, is facilitated by an internal ribosomal entry sequence (IRES). In addn., a custom-made IRES-lacZ cassette was also inserted downstream to HexA. These constructs correct enzyme deficiencies in vitro and can be used in the treatment of Tay-Sachs and Sandoff ***disease*** .

L6 ANSWER 12 OF 24 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2003:892558 CAPLUS
DN 139:376175
TI Vectors for expression of both isoforms of .beta.-hexosaminidase for use in lysosomal storage ***disease*** therapy
IN Kyrkanides, Stephanos
PA University of Rochester, USA
SO PCT Int. Appl., 132 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003092612	A2	20031113	WO 2003-US13672	20030502 <--
WO 2003092612	A3	20041104		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2483915	AA	20031113	CA 2003-2483915	20030502 <--
AU 2003234337	A1	20031117	AU 2003-234337	20030502 <--
EP 1501465	A2	20050202	EP 2003-728653	20030502

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

US 2004192630	A1	20040930	US 2004-781142	20040218
US 2006009406	A1	20060112	US 2004-978927	20041101

PRAI US 2002-377503P P 20020502
WO 2003-US13672 W 20030502

AB Disclosed herein are vectors and methods which solve the problems assocd. with enzyme replacement therapies directed to .beta.-hexosaminidase deficiencies. In accordance with the purposes of this invention, as embodied and broadly described herein, this invention, in one aspect, relates to ***vector*** constructs that comprise sequence encoding the HEX-.beta. and the HEX-.alpha. polypeptides. Also disclosed are vectors for perinatal gene delivery, including delivery of HEX-.alpha. and HEX-.beta., which can be used for inherited lysosomal disorders such as Tay-Sachs and Sandoffs ***disease*** . A bicistronic construct encoding for both isoforms of human .beta.-hexosaminidase, hHexA and hHexB was made (Figure 1). In this construct, the cytomegalovirus promoter (CMV) drives transgene expression, and the translation of the second open reading frame, HexB, is facilitated by an internal ribosomal entry sequence (IRES). An important property of the .beta.-Hex transgene is the products hhexA & hhexB have the ability to cross-correct, specifically, to be released extracellularly and then to be absorbed via paracrine pathways by other cells where by they contribute to .beta.-hexosaminidase activity. A tricistronic construct encoding for both isoforms of human 3-hexosaminidase, hHexA & hHexB, as well as the .beta.-galactosidase reporter gene (lacZ) was also made. In this construct, the cytomegalovirus promoter (CMV) drives transgene expression, and the translation of the second and third open reading frames (ORF), HexB and lacZ, resp., are facilitated by an internal ribosomal entry sequence (IRES). The tricistronic ***vector*** phexylacZ was stably expressed in embryonic hamster ***kidney*** fibroblasts (BHK-21; ATCC). Anal. of the transfected cells showed that cell lines (Crfk, ***spleen*** , ***brain*** , ***liver*** , and ***kidney***) stained pos. for X-gal, indicating expression of and translation of the expressed product from the tricistronic ***vector*** . The viral soln. was injected i.p. to 2 days old HexB-/- knockout mouse pups, which were allowed to reach the crit. age of 16 wk, when they displayed full signs of the lysosomal storage ***disease*** . It is important to state that at the crit. time point of 16 wk, the FIV(hex) injected mice showed statistically better locomotive performance compared to FIV(lacZ) injected mice (controls). Furthermore, the FIV(hex) mice had an extended life span for at least 2-3 addnl. weeks, at which point they were also terminated because they were showing signs of the ***disease*** .

L6 ANSWER 13 OF 24 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2003:837292 CAPLUS
DN 139:346783
TI Human and mouse cartilage differentiation regulating genes promoting type II collagen expression, and therapeutic and diagnostic use thereof
IN Matsuda, Akio; Honda, Goichi; Muramatsu, Shuji
PA Asahi Kasei Kabushiki Kaisha, Japan; Asahi Kasei Pharma Corporation
SO PCT Int. Appl., 271 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003087375	A1	20031023	WO 2003-JP4802	20030416 <--
WO 2003087375	C1	20050602		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2003223121	A1	20031027	AU 2003-223121	20030416 <--

PRAI JP 2002-113908 A 20020416
US 2002-373594P P 20020419
WO 2003-JP4802 W 20030416

AB The present invention provides the 32 protein promoting type II collagen expression useful in diagnosis, therapy and prophylaxis of diseases assocd. with cartilage impairments. Using the plasmid CPE43, the cDNA encoding a protein capable of promoting type II collagen expression has been cloned from the cDNA library constructed from mouse cell line ATDC5 and human ***lung*** fibroblast, and the DNA sequence and the deduced amino acid sequence were detd. The protein, the DNA encoding the protein, a recombinant ***vector*** contg. the DNA, and a transformant contg. the recombinant ***vector*** are useful in screening for a substance inhibiting or promoting the type II collagen expression.
RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 14 OF 24 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2003:698473 CAPLUS
DN 139:391689
TI Adenoviral VEGF-A gene transfer induces angiogenesis and promotes bone formation in healing osseous tissues
AU Tarkka, Tatu; Sipola, Annina; Jamsa, Timo; Soini, Ylermi; Yla-Herttuala, Seppo; Tuukkanen, Juha; Hautala, Timo
CS Department of Pharmacology and Toxicology, University of Oulu, FIN-90014, Finland
SO Journal of Gene Medicine (***2003***), 5(7), 560-566
CODEN: JGMEFG; ISSN: 1099-498X
PB John Wiley & Sons Ltd.
DT Journal
LA English
AB Background: Vascular endothelial growth factor (VEGF) is a key regulator of angiogenesis. VEGF has been safely and efficiently applied to stimulate neovascularization in ischemic tissues in atherosclerotic patients. VEGF has an important role in bone repair by promoting angiogenesis and by stimulating major skeletal cell populations, ***chondrocytes*** , osteoblasts and osteoclasts. Methods: We studied the effect of VEGF-A on the recovery of bone drilling defects in rat femur delivered with first-generation adenoviral ***vector*** . The virus

was injected into the ***muscle*** layer surrounding the bone defect made by drilling and the healing was followed for 1, 2, and 4 wk. Results: The VEGF effect was first demonstrated with an increased no. of FVIII-related antigen-pos. blood vessels in the defect area 1 wk after the procedure. The proportional area of remaining reparative tissue was significantly reduced in the VEGF-treated animals 2 wk after the injury suggesting favorable effect on bone healing. Increased periosteal cartilage was seen at the early phases of healing suggesting endochondral ossification. VEGF overexpression, however, completed the endochondral phase earlier compared with the control condition. Bone mineral content was enhanced in the VEGF-treated femurs measured with peripheral quant. computed tomog. at a 2-wk time point. Conclusions: Our data confirm the important role of VEGF in bone healing. We show for the first time that adenoviral VEGF-A gene transfer may modify bone defect healing in a rodent model.

RE.CNT 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 15 OF 24 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2003:574001 CAPLUS
DN 139:240767
TI Gene therapy for new bone formation using adeno-associated viral bone morphogenetic protein-2 vectors
AU Chen, Y.; Luk, K. D. K.; Cheung, K. M. C.; Xu, R.; Lin, M. C.; Lu, W. W.; Leong, J. C. Y.; Kung, H.-F.
CS Faculty of Medicine, Department of Orthopaedic Surgery, The University of Hong Kong, Hong Kong, Peop. Rep. China
SO Gene Therapy (***2003***), 10(16), 1345-1353
CODEN: GETHEC; ISSN: 0969-7128
PB Nature Publishing Group
DT Journal
LA English
AB Previous reports have suggested that bone morphogenetic protein (BMP) gene
therapy could be applied for in vivo bone regeneration. However, these studies were conducted either using immunodeficient animals because of immunogenicity of adenovirus vectors, or using ex vivo gene transfer technique, which is much more difficult to handle. Adeno-assocd. virus (AAV) is a replication-defective virus without any assocn. with immunogenicity and human ***disease*** . This study was conducted to investigate whether orthotopic new bone formation could be induced by in vivo gene therapy using AAV-based BMP2 vectors. To test the feasibility of this approach, the authors constructed an AAV ***vector*** carrying human BMP2 gene. Mouse myoblast cells (C2C12) transduced with this ***vector*** could produce and secrete biol. active BMP2 protein and induce osteogenic activity, which was confirmed by ELISA and alk. phosphatase activity assay. For in vivo study, AAV-BMP2 vectors were directly injected into the hindlimb ***muscle*** of immunocompetent Sprague-Dawley rats. Significant new bone under x-ray films could be detected as early as 3 wk postinjection. The ossification tissue was further examd. by histol. and immunohistochem. anal. This study is, to the authors' knowledge, the first to establish the feasibility of AAV-based BMP2 gene therapy for endochondral ossification in immunocompetent animals.

RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 16 OF 24 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2003:376136 CAPLUS
DN 138:362732
TI Therapeutic cell preparation grafts and methods of use thereof
IN Klein, Matthew B.; Cuono, Charles B.
PA USA
SO U.S. Pat. Appl. Publ., 16 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2003091543	A1	20030515	US 2002-44004	20020111 <--
PRAI US 2001-240570	A	20011026		

AB A biol. prepn. including genetically modified cells together with biocompatible matrixes and methods of use thereof are provided. The biol. prepn. is useful in treating a subject at risk for or suffering from a ***disease*** in a controllable dosage and time-dependent manner, and for in vitro and in vivo screening of candidate drug therapies. Gene therapy using Factor VIII transformed grafted human keratinocytes for treatment of hemophilia A is described.

L6 ANSWER 17 OF 24 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2003:97528 CAPLUS
DN 138:148683
TI Immortalization of human bone marrow stromal stem cells by retroviral ***vector*** comprising human telomeric repeat subunit gene
IN Thomas, G. Jensen; Moustapha, Kassem; Suresh, I. S. Rattan
PA Arhus Amt, Den.; Arhus Universitet
SO PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003010305	A1	20030206	WO 2002-DK514	20020726 <--
W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003049236	A1	20030313	US 2002-205629	20020726 <--
EP 1430115	A1	20040623	EP 2002-764564	20020726
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
PRAI DK 2001-1148	A	20010727		
US 2001-315939P	P	20010829		
WO 2002-DK514	W	20020726		

AB The present invention relates a method of immortalizing human bone marrow stem cells by transducing the cells with a retroviral ***vector*** comprising the human telomeric repeat subunit (hTRT) gene. The retroviral ***vector*** is driven by moloney murine leukemia virus long terminal repeat (GCSam). The immortalized stem cells may be used in the treatment of bone-fractures, bone loss assocd. with ageing and/or osteoporosis. The immortalized stem cells may be used in tissue engineering of bone, cartilage and skin matrix for treatment of none defects, cartilage defects and skin defects. The immortalized stem cells may be used in tissue engineering for producing growth factors, such as VEGF, PDGF and hGH. The immortalized stem cells may be used in prodn. of high amts. of pure protein for crystn.

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 18 OF 24 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2002:696159 CAPLUS
DN 137:246071
TI Gene expression profiles relating to normal and osteoarthritic cartilage
IN Liew, Choong-Chin; Marshall, Wayne E.; Zhang, Hongwei
PA Chondrogene Inc., Can.
SO PCT Int. Appl., 777 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 29

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002070737	A2	20020912	WO 2002-CA247	20020228 <--
WO 2002070737	C1	20021031		
WO 2002070737	C2	20031002		
WO 2002070737	A3	20040129		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2439504	AA	20020912	CA 2002-2439504	20020228 <--
AU 2002237124	A2	20020919	AU 2002-237124	20020228 <--
AU 2002237124	A9	20020919		
EP 1404868	A2	20040407	EP 2002-703416	20020228
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2002007657	A	20041026	BR 2002-7657	20020228
JP 2004536575	T2	20041209	JP 2002-570759	20020228
PRAI US 2001-271955P	P	20010228		
US 2001-275017P	P	20010312		
US 2001-305340P	P	20010713		
WO 2002-CA247	W	20020228		

AB The invention provides gene expression profiles comprising one or more polynucleotide sequences that are expressed in ***chondrocytes*** from any of the following developmental and ***disease*** stages: fetus, normal adult, mild osteoarthritis, moderate osteoarthritis, marked osteoarthritis, and severe osteoarthritis. Complementary DNA libraries were constructed from human fetal, normal, mild osteoarthritic and severe osteoarthritic cartilage samples (13,398, 17,151, 12,651, and 14,222 expressed sequence tags (ESTs), resp.). The known and novel clones derived from these libraries were then used to construct human ***chondrocyte*** -specific microarrays to generate differential gene expression profiles useful as a diagnostic tools for detection of osteoarthritis. A total of 5807 expressed gene sequences are provided and matched to known gene sequences, other ESTs, or mitochondrial, ribosomal, ***vector*** , and cDNA/hypothetical protein sequences in the public databases. Arrays of the invention are useful as a gold std. for osteoarthritis diagnosis and for use to identify and monitor therapeutic

efficacy of new drug targets.

L6 ANSWER 19 OF 24 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2002:1005 CAPLUS
DN 136:145551
TI Fibroblast-mediated delivery of growth factor complementary DNA into mouse joints induces chondrogenesis but avoids the disadvantages of direct viral gene transfer
AU Gelse, K.; Jiang, Q.-J.; Aigner, T.; Ritter, T.; Wagner, K.; Poschl, E.; von der Mark, K.; Schneider, H.
CS Department of Experimental Medicine I, University of Erlangen-Nuremberg, Erlangen, 91054, Germany
SO Arthritis & Rheumatism (***2001***), 44(8), 1943-1953
CODEN: ARHEAW; ISSN: 0004-3591
PB Wiley-Liss, Inc.
DT Journal
LA English
AB To assess the advantages and disadvantages of a direct adenoviral and a cell-mediated approach to the induction of cartilage formation in joints by transfer of growth factor genes. Adenoviral vectors carrying insulin-like growth factor 1 (IGF-1) or bone morphogenetic protein 2 (BMP-2) cDNA were constructed and applied to primary human and murine ***chondrocytes*** or fibroblasts. Transgene expression was quantified by ELISA. Direct injection of these vectors or AdLacZ, a reporter gene ***vector*** , into mouse knee joints was compared with the transplantation of syngeneic fibroblasts (infected ex vivo with the same vectors) with respect to virus spread, immune response, and cartilage formation by use of histol., immunohistochem., and mol. analyses. AdIGF-1 and AdBMP-2 efficiently infected all cell types tested. Human cells secreted biol. relevant levels of protein over a period of at least 28 days. Direct transfer of AdLacZ into mouse knee joints resulted in pos. stained synovial tissues, whereas AdLacZ-infected fibroblasts settled on the surface of the synovial membranes. Inadvertent spread of ***vector*** DNA into the ***liver*** , ***lung*** , and ***spleen*** was identified by nested polymerase chain reaction in all mice that had received the ***vector*** directly; this rarely occurred following fibroblast-mediated gene transfer. Direct injection of AdBMP-2 induced the synthesis of new cartilage in periarticular mesenchyme, accompanied by extensive osteophyte formation. When AdBMP-2 was administered by injecting ex vivo-infected fibroblasts, cartilage formation was obsd. only in regions near the injected cells. AdIGF-1 treatment did not lead to morphol. changes. Importantly, fibroblast-mediated gene transfer avoided the strong immune response to adenovirus that was elicited following direct application of the ***vector*** . The authors' results indicate that cell-mediated gene transfer provides sufficient BMP-2 levels in the joint to induce cartilage formation while avoiding inadvertent ***vector*** spread and immune reactions.
RE.CNT 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 20 OF 24 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2001:868632 CAPLUS
DN 136:17050
TI Intraflagellar transport particle polypeptides of Chlamydomonas and their uses in diagnosis and treatment of ***disease***
IN Witman, George B.; Pazour, Gregory J.; Rosenbaum, Joel L.; Cole, Douglas G.
PA University of Massachusetts, USA
SO PCT Int. Appl., 132 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001090307	A2	20011129	WO 2001-US17103	20010524 <--
WO 2001090307	A3	20020418		
WO 2001090307	C2	20021010		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2410566	AA	20011129	CA 2001-2410566	20010524 <--
AU 2001069714	A5	20011203	AU 2001-69714	20010524 <--
US 2002127620	A1	20020912	US 2001-866582	20010524 <--
EP 1339423	A2	20030903	EP 2001-948242	20010524 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2005054842	A1	20050310	US 2004-839016	20040505
PRAI US 2000-206923P	A2	20000524		
US 2001-866582	B1	20010524		
WO 2001-US17103	W	20010524		

AB The invention relates to various Chlamydomonas intraflagellar transport (IFT) polypeptides and the nucleic acids that encode them. These IFT particle polypeptides and nucleic acids can be used in a variety of diagnostic, screening, and therapeutic methods for ***kidney*** ***disease*** , retinal disorders, thyroid disorders, ***chondrocyte*** ***disease*** , olfactory ***disease*** , azoospermia or primary ciliary dyskinesia. The present invention has implications involving treating an infection caused by a nematode, insect, protozoa or bacteria in a human, animal or plant by inhibiting function of an IFT particle polypeptide in the pathogen.

L6 ANSWER 21 OF 24 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2000:881315 CAPLUS
DN 134:55504
TI Suppressor of cytokine signaling SOCS-3 promoter and methods for its use
IN Auernhammer, Christoph J.; Shlomo, Melmed
PA Cedars-Sinai Medical Center, USA
SO PCT Int. Appl., 64 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000075326	A1	20001214	WO 2000-US40151	20000606 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6541244	B1	20030401	US 1999-327138	19990607 <--
CA 2376663	AA	20001214	CA 2000-2376663	20000606 <--
US 2002166136	A1	20021107	US 2002-124905	20020417 <--
US 2002174448	A1	20021121	US 2002-136224	20020429 <--
US 6943018	B2	20050913		
US 2003186286	A1	20031002	US 2002-334385	20021231 <--
US 2005172346	A1	20050804	US 2005-93079	20050329
US 2005188429	A1	20050825	US 2005-92026	20050329
PRAI US 1999-327138	A	19990607		
WO 2000-US40151	W	20000606		
US 2002-136224	A3	20020429		

AB Disclosed is a nucleic acid construct comprising a murine SOCS-3 promoter sequence having SEQ. ID.NO.:1, or a non-murine homolog thereof, or an operative fragment or deriv. The construct can also contain, operatively linked to the SOCS-3 promoter, a gene encoding any preselected protein, and optionally contains a reporter gene to facilitate detection and/or selection of successfully transfected cells. Also disclosed are a transgenic vertebrate cell contg. the nucleic acid construct and transgenic non-human vertebrates comprising such cells. The nucleic acid construct is useful in methods of treating a growth retardation or growth acceleration ***disorder*** in a human subject and in a method of treating an autoimmune ***disease*** , immune ***disease*** , or inflammatory condition in a human subject. A kit for genetically modifying a vertebrate cell includes a polynucleotide comprising the murine SOCS-3 promoter sequence is also disclosed.
RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 22 OF 24 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2000:68485 CAPLUS
DN 132:117957
TI Human neurotrophic growth factor enovin and its encoding nucleic acids and biological activities
IN Geerts, Hugo Alfonso; Masure, Stefan Leo Jozef; Meert, Theo Frans; Cik, Miroslav; Ver Donck, Luc August Laurentius
PA Janssen Pharmaceutica N.V., Belg.
SO PCT Int. Appl., 125 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000004050	A2	20000127	WO 1999-EP5031	19990714 <--
WO 2000004050	A3	20001109		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2333910	AA	20000127	CA 1999-2333910	19990714 <--
AU 9952832	A1	20000207	AU 1999-52832	19990714 <--
AU 768472	B2	20031211		
BR 9912819	A	20010502	BR 1999-12819	19990714 <--
EP 1097167	A2	20010509	EP 1999-938261	19990714 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
TR 200100074	T2	20011121	TR 2001-200100074	19990714 <--
JP 2002520042	T2	20020709	JP 2000-560156	19990714 <--

NZ 509723 A 20040130 NZ 1999-509723 19990714
RU 2238947 C2 20041027 RU 2001-104351 19990714
EP 1640381 A2 20060329 EP 2005-112473 19990714
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, AL, BA, HR, YU
BG 105107 A 20011031 BG 2001-105107 20010103 <--
ZA 2001000330 A 20020111 ZA 2001-330 20010111 <--
NO 2001000212 A 20010314 NO 2001-212 20010112 <--
HR 2001000036 A1 20011231 HR 2001-36 20010112 <--
US 2005233359 A1 20051020 US 2005-74498 20050308
US 2006122135 A1 20060608 US 2005-74497 20050308
PRAI GB 1998-15283 A 19980714
US 1999-248772 A 19990212
US 1999-327668 A 19990608
EP 1999-938261 A3 19990714
US 1999-357349 A1 19990714
WO 1999-EP5031 W 19990714

AB There is disclosed an isolated nucleic acid mol. encoding a human neurotrophic growth factor designated enovin and its deduced amino acid sequence(s). At least 5 splice variants of enovin are identified, generally differing in the precursor moiety. The mature growth factor preferably comprises 113 amino acid residues, or functional equivs., derivs. or bioprecursors thereof. The gene encoding enovin is localized to human chromosome 1p31.3-p32. Enovin demonstrates in vitro effects on neurite outgrowth, protection against taxol-induced neurotoxicity in stauroporine-differentiated SH-Sy5Y human neuroblastoma cell cultures, and binds to glial cell-derived neurotrophic factor receptor .alpha.-3. Enovin mRNA is expressed ubiquitously, with the highest levels in prostate, pituitary gland, trachea, placenta, fetal ***lung*** , ***pancreas*** , and ***kidney*** . The nucleic acid mol. encoding enovin can be used to transform a host cell, tissue or organism by including it in an appropriate ***vector*** . The host cell, tissue or organism and the ***vector*** also form part of the invention.

L6 ANSWER 23 OF 24 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1999:194251 CAPLUS
DN 130:233257
TI Improved method of infecting cells with adenoviral vectors and therapeutic uses thereof
IN Feldmann, Marc; Foxwell, Brian Maurice John; Brennan, Fionula Mary; Bondeson, Jan
PA The Mathilda and Terence Kennedy Institute of Rheumatology, UK
SO PCT Int. Appl., 77 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9913064	A2	19990318	WO 1998-GB2753	19980911 <--
WO 9913064	A3	19990617		
W: JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 1012321	A2	20000628	EP 1998-942892	19980911 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001515716	T2	20010925	JP 2000-510853	19980911 <--
US 2002177572	A1	20021128	US 2001-33267	20011025 <--
PRAI GB 1997-19238	A	19970911		
WO 1998-GB2753	W	19980911		
US 2000-508350	B1	20000407		

AB The invention provides an in vitro method for infecting one or more cells with a viral ***vector*** capable of transporting exogenous or recombinant nucleic acid into the cells to be infected. In one embodiment, cells are treated with a cytokine prior to infection to increase the expression of cell surface integrins .alpha.V.beta.3 and .alpha.V.beta.5, which are required for viral entry into the cell. In another embodiment, the cells are infected with a replication-deficient viral ***vector*** such as an adenovirus. A method of infecting rheumatoid synovial cells and other cells comprising high levels of cell surface integrins is also disclosed. Adenovirus is known to be used in gene therapy, but its use in the treatment of inflammatory diseases such as rheumatoid arthritis, asthma, chronic obstructive pulmonary ***disease*** , Crohn's ***disease*** , and ulcerative colitis is novel to the invention.

L6 ANSWER 24 OF 24 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1998:794982 CAPLUS
DN 130:21344
TI Mammalian cell transduction for use in gene therapy for hemophilia A
IN Vanden, Driessche Thierry; Chuah, Marinee Khim Lay
PA Leuven Research & Development Vzw, Belg.
SO PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9853063	A2	19981126	WO 1998-EP3013	19980518 <--
WO 9853063	A3	19990318		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
EP 938904	A1	19990901	EP 1998-200382	19980209 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
CA 2289918	AA	19981126	CA 1998-2289918	19980518 <--
AU 9881057	A1	19981211	AU 1998-81057	19980518 <--
EP 980264	A2	20000223	EP 1998-930718	19980518 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
PRAI EP 1997-201480	A	19970516		
EP 1998-200382	A	19980209		
WO 1998-EP3013	W	19980518		

AB The present invention relates to a method for the ex vivo transduction of mammalian cells, in particular to the transduction of bone marrow stromal cells. These cells can be transduced with a gene of interest, in particular a B-domain deleted human factor VIII gene. In the latter case, the transduced cells can be used to treat hemophilia A. The method for the ex vivo transduction of bone marrow stromal cells with the human factor VIII gene comprises provision of an intron-based retroviral ***vector*** comprising a B-domain deleted human factor VIII cDNA (designated as MFG-FVIII.DELTA.B); pseudotyping the said ***vector*** with the Gibbon ape leukemia virus (GALV) envelope; transducing bone marrow stromal cells with the said pseudotyped ***vector*** by pre-incubating the cells for a suitable period of time in cell culture medium without phosphate and subsequently adding a ***vector*** -contg. supernatant, optionally supplemented with transduction additives to the cells, followed by centrifuging the mixt. thus obtained; and optionally repeating the two previous steps. An advantage of the method is that no myeloablation is required. Because of this, the gene therapeutic method described is clin. acceptable for hemophilia patients. A large no. of FVIII expressing primary BM stromal cells could be obtained while obviating the need to enrich for transduced cells by selection and without inducing stromal cell proliferation by supplementing high doses of exogenous purified growth factors. These improvements shorten the in vitro culture period of the BM stromal cells that are thus more likely to retain their original properties. Furthermore, since selective enrichment of transduced cells was not needed, it was not necessary to include a neoR selectable marker in the ***vector*** .

=> d his

(FILE 'HOME' ENTERED AT 17:12:15 ON 15 JUN 2006)

FILE 'EMBASE, BIOSIS, CAPLUS' ENTERED AT 17:12:33 ON 15 JUN 2006
L1 34642 S CHONDROCYTE?
L2 564 S L1 AND VECTOR
L3 163 S L2 AND (DISORDER OR DISEASE)
L4 131 DUP REM L3 (32 DUPLICATES REMOVED)
L5 80 S L4 AND PY<=2003
L6 24 S L5 AND (BRAIN OR HEART OR LIVER OR KIDNEY OR GASTRO INTESTIN

=> s l1 (3s) vector
L7 361 L1 (3S) VECTOR

=> s l7 and gel
L8 21 L7 AND GEL

=> dup rem l8
PROCESSING COMPLETED FOR L8
L9 11 DUP REM L8 (10 DUPLICATES REMOVED)

=> d bib abs 1-
YOU HAVE REQUESTED DATA FROM 11 ANSWERS - CONTINUE? Y/(N):y

L9 ANSWER 1 OF 11 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN
AN 2006191531 EMBASE
TI Reconstruction of tissue engineered cartilage with BMP7 gene transfected chondrocytes.
AU Qu F.-J.; Hou Y.; Liu L.-L.; Zhou Y.-L.; Hou L.-Z.
CS Prof. L.-Z. Hou, Institute of Frontier Medical Science, Jilin University, Changchun 130021 Jilin Province, China
SO Chinese Journal of Clinical Rehabilitation, (10 Apr 2006) Vol. 10, No. 13, pp. 59-61. .
Refs: 3
ISSN: 1671-5926 CODEN: ZLKHAH
CY China
DT Journal; Article
FS 022 Human Genetics
029 Clinical Biochemistry
LA Chinese
SL English; Chinese
ED Entered STN: 18 May 2006
Last Updated on STN: 18 May 2006
AB Aim: To construct tissue engineering cartilage transfected with BMP7 gene,

determine the expression of BMP7 gene in the tissue engineering cartilage and probe into the biological difference between transfected and non-transfected with BMP7 gene in biology. Methods: This experiment was conducted at the Institute of Clinical Pharmacy and Pharmacolog, Second Hospital Affiliated to Harbin Medical University from June 2004 to January 2005. We used the recombinant pcDNA3.1-BMP7 eukaryotic expression ***vector*** plasmid and screened positive clones with G(418) for 14 days. Collagen-fibrin ***gel*** composite was used to construct tissue engineering cartilage transfected with BMP7 gene. Tissue engineering cartilage non-transfected with BMP7 gene was used as control. The inoculated density of ***chondrocytes*** was 5x10(9) L(-1). The culture of tissue engineering cartilage was given histological analysis with Toluidine blue, hematoxylin-eosin staining; The expression of type II collagen mRNA was detected with in situ hybridization; The microstructure of the culture of tissue engineering cartilage was observed under the transmission electron microscope; The expression of BMP7 mRNA and protein cultured in vitro were measured with in situ hybridization and immunohistochemical staining. Results: 1 Chondrocytes transfected with BMP7 gene: After screened with G418, a lot of cells died and about 30% cells survived and grew. Positive clone cells appeared after 14- and 28-day consecutive screening with G(418), and the rate of adhesion grow was 100%. The survived positive clone cells were chondrocytes transfected successfully. 2 Morphology of tissue engineering cartilage culture and observation results under the microscope: The culture of constructed tissue engineering cartilage presented light pink ***gel*** -like, round plate in shape, transparent, and 16 mmx16 mmx3 mm in volume. Only a round thin cell layer was observed under the microscope. 3 Histological analysis of the culture of tissue engineering cartilage: After the culture of tissue engineering cartilage was cultured in vitro for 7, 14 and 28 days, much extracellular matrix was around the cells. There was much cellular matrix in the culture of tissue engineering cartilage transfected with BMP7 gene. The synthesis and secretion of chondrocytes were the most active after in vitro culture for 14 days. 4 Detection of in situ hybridization of mRNA expressed by Type II collagen: The peripheral area of the cellular nucleus of chondrocytes was yellow brown, and mRNA was also expressed. 5 DNA content of tissue engineering cartilage culture increased gradually with the prolonging of culture time, reached the top on day 21. DNA content of the culture of tissue engineering cartilage was higher transfected with BMP7 gene than non-transfected with BMP7 gene ($P < 0.05$). 6 The content of glycosaminoglycan of tissue engineering cartilage culture transfected with BMP7 gene was the highest on day 14, and the content of glycosaminoglycan was higher transfected with BMP7 gene than non-transfected with BMP7 gene at each time point ($P < 0.05$). 7 As compared with tissue engineering cartilage transfected with BMP7 gene, after in vitro culture for 7 days, organelle of the cartilage culture transfected with BMP7 gene was developed, and endoplasmic reticulum, mitochondrion and dictyosome were relatively abundant. Cellular matrix sysnthesis was much vigorous; After in vitro culture for 21 days, rough endoplasmic reticulum of the cartilage transfected with BMP7 gene was still developed, but mitochondrion and dictyosome were relatively decreased, and the synthetic ability of cellular matrix was attenuated. 8 After in vitro culture for 7, 14 and 21 days, BMP7 mRNA expression appeared in the chondrocytes of tissue engineering cartilage culture transfected with BMP7 gene, but did not appeared in the cartilage culture non-transfected with BMP7 gene. 9 Immunohistochemical detection of BMP7 protein expression showed that after in vitro culture for 7, 14 and 21 days, BMP7 protein expression appeared in all the chondrocytes of the culture of tissue engineering cartilage transfected with BMP7 gene, but not appeared in the chondrocytes of the culture non-transfected with BMP7 gene. Conclusion: Tissue engineering cartilage transfected with BM P7 gene is constructed successfully. Its biological characteristics are superior to those of cartilage non-transfected with BMP7. It has certain feasibility and superiority to repair cartilage tissue defect with tissue engineering cartilage transfected with BMP7 gene.

L9 ANSWER 2 OF 11 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN DUPLICATE 1
AN 2005120350 EMBASE
TI The role of Galectin-1 in the interaction between chondrocytes and a lactose-modified chitosan.
AU Marcon P.; Marsich E.; Vetere A.; Mozetic P.; Campa C.; Donati I.; Vittur F.; Gamini A.; Paoletti S.
CS A. Vetere, Dept. Biochem., Biophys. M., University of Trieste, Via L. Giorgieri 1, I-34127 Trieste, Italy. vetere@bbcm.univ.trieste.it
SO Biomaterials, (2005) Vol. 26, No. 24, pp. 4975-4984. .
Refs: 50
ISSN: 0142-9612 CODEN: BIMADU
CY United Kingdom
DT Journal; Article
FS 022 Human Genetics
027 Biophysics, Bioengineering and Medical Instrumentation
029 Clinical Biochemistry
LA English
SL English
ED Entered STN: 7 Apr 2005
Last Updated on STN: 7 Apr 2005
AB Evidences for the involvement of the Galectin-1 in the interaction of pig chondrocytes with a lactose-modified chitosan, namely Chitlac, are reported. The Chitlac glycopolymer has been shown to promote pig ***chondrocyte*** aggregation and to induce extracellular matrix production. Highly pure Galectin-1 was obtained from pig spleen by affinity chromatography and its identity was determined by ion spray mass spectrometry analysis of tryptic peptide fragments obtained after in-***gel*** digestion. The complete sequence of pig Galectin-1 CDS was obtained by screening a pig EST database using human Galectin-1 sequence as template. The Galectin-1 cDNA was cloned into a pGEX-4T-1 expression ***vector*** and the recombinant protein was purified, characterized and used to produce a rabbit anti-serum. Recombinant Galectin-1 interacts in a dose-dependent manner with Chitlac as determined with ELISA assay. Expression level of galectin-1 gene, quantified by real-time PCR, was significantly higher in ***chondrocytes*** cultivated on Chitlac. In the same way, the presence of Chitlac stimulates secretion of Galectin-1 in culture medium that, by immunohistochemical analysis, revealed to be clustered on the surface of Chitlac-induced aggregates. These data indicate the role of Galectin-1 as a bridging agent between Chitlac and chondrocyte aggregates.

L9 ANSWER 3 OF 11 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN
AN 2005170950 EMBASE
TI Continuous transforming growth factor .beta.(1) secretion by cell-mediated gene therapy maintains chondrocyte redifferentiation.
AU Lee D.K.; Choi K.B.; Oh I.S.; Song S.U.; Hwang S.; Lim C.-L.; Hyun J.-P.; Lee H.-Y.; Chi G.F.; Yi Y.; Yip V.; Kim J.; Lee E.B.; Noh M.J.; Lee K.H.
CS Dr. D.K. Lee, TissueGene, Inc., Gaithersburg, MD 20877, United States. dklee@tissuegene.com
SO Tissue Engineering, (2005) Vol. 11, No. 1-2, pp. 310-318. .
Refs: 41
ISSN: 1076-3279 CODEN: TIENFP
CY United States
DT Journal; Article
FS 022 Human Genetics
026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
037 Drug Literature Index
LA English
SL English
ED Entered STN: 12 May 2005
Last Updated on STN: 12 May 2005
AB One of the most important factors in the production of cartilage is transforming growth factor .beta.(1) (TGF-.beta.(1)). To obtain sustained release of TGF-.beta.(1), a cell-mediated gene therapy technique was introduced. We infected ***chondrocytes*** with a retroviral ***vector*** carrying the TGF-.beta.(1) gene. The single clone derivative showed sustained TGF-.beta.(1) secretion. It also showed constitutive type II collagen expression. Whereas the TGF-.beta.(1) protein itself is unable to induce formation of cartilage in vivo, human ***chondrocytes*** engineered to express a retroviral ***vector*** encoding TGF-.beta.(1) showed cartilage formation in vivo when cells were injected into nude mice intradermally. These data suggest that cell-mediated gene therapy using TGF-.beta.(1) as a transgene would be a promising treatment for osteoarthritis.

L9 ANSWER 4 OF 11 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN
AN 2005452004 EMBASE
TI Long-term gene expression using the lentiviral ***vector*** in rat ***chondrocytes*** .
AU Lu F.-Z.; Kitazawa Y.; Hara Y.; Jiang J.-Y.; Li X.-K.
CS Dr. X.-K. Li, Laboratory of Transplantation Immunology, National Research Institute for Child Health and Development, 2-10-1 Okura, Setagaya-ku Tokyo 157-8535, Japan. sri@nch.go.jp
SO Clinical Orthopaedics and Related Research, (2005) No. 439, pp. 243-252. .
Refs: 36
ISSN: 0009-921X CODEN: CORTBR
CY United States
DT Journal; Article
FS 022 Human Genetics
033 Orthopedic Surgery
037 Drug Literature Index
LA English
SL English
ED Entered STN: 17 Nov 2005
Last Updated on STN: 17 Nov 2005
AB The optimal approach to a long-term stable transgene expression in chondrocytes has not been established. Recently, lentiviral vectors have been used for transfection of some cultured cell lines. Our study tests the hypothesis that lentiviral vectors lead to longer gene expression in primary chondrocytes. We transfected lentiviral and adenoviral vectors carrying the green fluorescence protein gene to chondrocytes at different infection rates and cultured them in collagen Type I ***gel*** for up to 6 weeks. We also transplanted the cells of ***gel*** -suspended ***chondrocytes*** into the backs of nude mice. The mRNA expression of collagen Type II and aggrecan core protein was tested by real time polymerase chain reaction. The morphologic features and proliferation of ***chondrocytes*** were observed. Lentiviral vectors could transfect the green fluorescence protein gene to ***chondrocytes*** and the adenoviral ***vector*** , and there was no influence on the proliferation and phenotype of the ***chondrocytes*** . The percentage of lentiviral green fluorescence protein positive cells was much greater than the adenoviral green fluorescence protein at the end of 6 weeks. Stable green fluorescence protein expression was observed only in the lentivirus-transfected implants. The gene transfected by the lentiviral ***vector*** can be expressed efficiently for a long time and may be useful for gene transfer in cartilage defect repair.

L9 ANSWER 5 OF 11 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN DUPLICATE 2
AN 2005042644 EMBASE
TI Repair of articular cartilage defect by autologous transplantation of basic fibroblast growth factor gene-transduced ***chondrocytes*** with adeno-associated virus ***vector*** .
AU Yokoo N.; Saito T.; Uesugi M.; Kobayashi N.; Xin K.-Q.; Okuda K.; Mizukami H.; Ozawa K.; Koshino T.
CS Dr. N. Yokoo, Department of Orthopaedic Surgery, Yokohama City Univ. Sch. of Medicine, 3-9 Fukuura, Kanazawa-ku, Yokohama 236-0004, Japan. Napoleon@nyc.odn.ne.jp
SO Arthritis and Rheumatism, (2005) Vol. 52, No. 1, pp. 164-170. .
Refs: 25
ISSN: 0004-3591 CODEN: ARHEAW
CY United States
DT Journal; Article
FS 022 Human Genetics
031 Arthritis and Rheumatism
037 Drug Literature Index
LA English
SL English
ED Entered STN: 4 Feb 2005
Last Updated on STN: 4 Feb 2005
AB Objective. To examine the effects of basic fibroblast growth factor (bFGF) gene-transduced ***chondrocytes*** on the repair of articular cartilage defects. Methods. LacZ gene or bFGF gene was transduced into primary isolated rabbit ***chondrocytes*** with the use of a recombinant adeno-associated virus (AAV) ***vector*** . These gene-transduced ***chondrocytes*** were embedded in collagen ***gel*** and transplanted into a full-thickness defect in the articular cartilage of the patellar groove of a rabbit. The efficiency of gene transduction was assessed according to the percentage of LacZ-positive cells among the total number of living cells. The concentration of bFGF in the culture supernatant was measured by enzyme-linked immunosorbent assay to confirm the production by bFGF gene-transduced ***chondrocytes*** . At 4, 8, and 12 weeks after transplantation, cartilage repair was evaluated histologically and graded semiquantitatively using a histologic scoring system ranging from 0 (complete regeneration) to 14 (no regeneration) points. Results. LacZ gene expression by chondrocytes was maintained until 8 weeks in >85% of the in vitro population. LacZ-positive cells were found at the transplant sites for at least 4 weeks after surgery. The mean concentration of bFGF was significantly increased in bFGF gene-transduced cells compared with control cells ($P < 0.01$). Semiquantitative histologic scoring indicated that the total score was significantly lower in the bFGF-transduced group than in the control group throughout the observation period. Conclusion. These results demonstrated that gene transfer to ***chondrocytes*** by an ex vivo method was established with the AAV ***vector*** , and transplantation of bFGF gene-transduced ***chondrocytes*** had a clear beneficial effect on the repair of rabbit articular cartilage defects.

L9 ANSWER 6 OF 11 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN DUPLICATE 3
AN 2004296122 EMBASE
TI Peroxisome proliferator-activated receptor-.gamma. down-regulates chondrocyte matrix metalloproteinase-1 via a novel composite element.
AU Francois M.; Richette P.; Tsagris L.; Raymondjean M.; Fulchignoni-Lataud M.-C.; Forest C.; Savouret J.-F.; Corvol M.-T.
CS M.-T. Corvol, INSERM UMR-S-530, Universite Paris 5, UFR Biomedicale, 45 Rue des Saints Peres, 75006 Paris, France. maite.corvol@univ-pacis5.fr
SO Journal of Biological Chemistry, (2 Jul 2004) Vol. 279, No. 27, pp. 28411-28418. .
Refs: 48
ISSN: 0021-9258 CODEN: JBCHA3
CY United States
DT Journal; Article
FS 029 Clinical Biochemistry
037 Drug Literature Index
LA English
SL English
ED Entered STN: 12 Aug 2004
Last Updated on STN: 12 Aug 2004
AB Interleukin-1.beta. (IL-1.beta.) induces degradation via hyperexpression of an array of genes, including metalloproteinases (MMP), in cartilage cells during articular degenerative diseases. In contrast, natural ligands for peroxisome proliferator-activated receptors (PPARs) display protective anti-cytokine effects in these cells. We used the PPAR agonist rosiglitazone (Rtz) to investigate PPAR-.gamma. isotype on IL-1.beta.-target genes. Immunocytochemistry, electrophoretic mobility shift, and transient transfection assays revealed a functional PPAR-.gamma. in chondrocytes in vitro. Rtz displayed significant inhibition of IL-1.beta. effects in ***chondrocytes*** . Low Rtz concentrations (close to K(d) values for PPAR-.gamma., 0.1 to .mu.M) inhibited the effects of IL-1.beta. on (35)S-sulfated proteoglycan production and gelatinolytic activities and down-regulated MMP1 expression at mRNA and protein levels. We have investigated the mechanism of action of Rtz against IL-1.beta.-mediated MMP1 gene hyperexpression. Rtz effect occurs at the transcriptional level of the MMP1 promoter, as observed in transiently transfected cells with pMMP1-luciferase ***vector*** . Transient expression of wild type PPAR-.gamma. enhanced Rtz inhibitory effect in ***chondrocytes*** , whereas a mutated dominant negative PPAR-.gamma. abolished it, supporting the role of PPAR-.gamma. In this effect. MMP1 gene promoter analysis revealed the involvement of a cis-acting element located at -83 to -77, shown to be a composite PPRE/AP1 site. ***Gel*** mobility and supershift assays demonstrated that PPAR-.gamma. and c-Fos/c-Jun proteins bind this cis-acting element in a mutually exclusive way. Our data high light a new PPAR-.gamma.-dependent inhibitory mechanism on IL-1.beta.-mediated cartilage degradation occurring through DNA binding competition on the composite PPRE/AP1 site in the MMP1 promoter.

L9 ANSWER 7 OF 11 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN
AN 2003190901 EMBASE
TI Responses to the proinflammatory cytokines interleukin-1 and tumor necrosis factor .alpha. in cells derived from rheumatoid synovium and other joint tissues involve nuclear factor .kappa.B-mediated induction of the Ets transcription factor ESE-1.
AU Grall F.; Gu X.; Tan L.; Cho J.-Y.; Inan M.S.; Pettit A.R.; Thamrongsak U.; Choy B.K.; Manning C.; Akbarali Y.; Zerbini L.; Rudders S.; Goldring S.R.; Gravallese E.M.; Oettgen P.; Goldring M.B.; Libermann T.A.
CS Dr. T.A. Libermann, New England Baptist Bone/Jt. Inst., Department of Medicine, Beth Israel Deaconess Medical Center, 4 Blackfan Circle, Boston, MA 02115, United States. tliberma@bidmc.harvard.edu
SO Arthritis and Rheumatism, (1 May 2003) Vol. 48, No. 5, pp. 1249-1260. .
Refs: 53
ISSN: 0004-3591 CODEN: ARHEAW
CY United States
DT Journal; Article
FS 005 General Pathology and Pathological Anatomy
026 Immunology, Serology and Transplantation
031 Arthritis and Rheumatism
LA English
SL English
ED Entered STN: 29 May 2003
Last Updated on STN: 29 May 2003
AB Objective. To investigate the expression of the novel Ets transcription factor ESE-1 in rheumatoid synovium and in cells derived from joint tissues, and to analyze the role of nuclear factor .kappa.B (NF-.kappa.B) as one of the central downstream targets in mediating the induction of ESE-1 by proinflammatory cytokines. Methods. ESE-1 protein expression was analyzed by immunohistochemistry using antibodies in synovial tissues from patients with rheumatoid arthritis (RA) and osteoarthritis (OA). ESE-1 messenger RNA (mRNA) levels were analyzed by reverse transcriptase-polymerase chain reaction or Northern blotting in human ***chondrocytes*** , synovial fibroblasts, osteoblasts, and macrophages, before and after exposure to interleukin-1.beta. (IL-1.beta.), tumor necrosis factor a (TNFa), or lipopolysaccharide (LPS) with or without prior infection with an adenovirus encoding the inhibitor of nuclear factor .kappa.B (I.kappa.B). The wild-type ESE-1 promoter and the ESE-1 promoter mutated in the NF-.kappa.B site were cloned into a luciferase reporter ***vector*** and analyzed in transient transfections. Electrophoretic mobility shift assays (EMSAs) and supershift assays with antibodies against members of the NF.kappa.B family were conducted using the NF-.kappa.B site from the ESE-1 promoter as a probe. Results. Immunohistochemical analysis showed specific expression of ESE-1 in cells of the synovial lining layer and in some mononuclear and endothelial cells in RA and OA synovial tissues. ESE-1 mRNA expression could be induced by IL-1.beta. and TNF.alpha. in cells such as synovial fibroblasts, ***chondrocytes*** , osteoblasts, and monocytes. Transient transfection experiments and EMSAs showed that induction of ESE-1 gene expression by IL-1.beta. requires activation of NF.kappa.B and binding of p50 and p65 family members to the NF.kappa.B site in the ESE-1 promoter. Overexpression of I.kappa.B using an adenoviral ***vector*** blocked IL-1.beta.-induced ESE-1 mRNA expression. Chromatin immunoprecipitation further confirmed that NF-.kappa.B binds to the ESE-1 promoter in vivo. Conclusion. ESE-1 is expressed in synovial tissues in RA and, to a variable extent, in OA, and is specifically induced in synovial fibroblasts, chondro cytes, osteoblasts, and monocyte/macrophages by IL-1ss, TNF.kappa., or LPS. This induction relies on the translocation of the NF-KB family members p50 and p65 to the nucleus and transactivation of the ESE-1 promoter via a high-affinity NF-.kappa.B binding site. ESE-1 may play a role in mediating some effects of proinflammatory stimuli in cells at sites of inflammation.

L9 ANSWER 8 OF 11 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN DUPLICATE 4
AN 2005101936 EMBASE
TI Sustained transgene expression in cartilage defects in vivo after transplantation of articular chondrocytes modified by lipid-mediated gene transfer in a ***gel*** suspension delivery system.
AU Madry H.; Cucchiarini M.; Stein U.; Remberger K.; Menger M.D.; Kohn D.; Trippel S.B.
CS H. Madry, Lab. for Experimental Orthopaedics, Department of Orthopaedic Surgery, Saarland University Medical Center, 66421 Homburg, Germany. hmad@hotmail.com
SO Journal of Gene Medicine, (2003) Vol. 5, No. 6, pp. 502-509. .
Refs: 29
ISSN: 1099-498X CODEN: JGMEFG
CY United Kingdom
DT Journal; Article
FS 022 Human Genetics
031 Arthritis and Rheumatism
037 Drug Literature Index
039 Pharmacy

LA English
SL English
ED Entered STN: 17 Mar 2005
Last Updated on STN: 17 Mar 2005
AB Background: Genetically modified ***chondrocytes*** may be able to modulate articular cartilage repair. To date, transplantation of modified ***chondrocytes*** into cartilage defects has been restricted to viral vectors. We tested the hypothesis that a recombinant gene can be delivered to sites of cartilage damage in vivo using ***chondrocytes*** transfected by a lipid-mediated gene transfer method. Methods: Isolated lapine articular ***chondrocytes*** were transfected with an expression plasmid ***vector*** carrying the P. pyralis luciferase gene using the reagent FuGENE 6. Transfected ***chondrocytes*** were encapsulated in alginate spheres and implanted into osteochondral defects in the knee joints of rabbits. Results: In vitro, luciferase activity in pCMVLuc-transfected spheres showed an early peak at day 2 post-transfection and remained elevated at day 32, the longest time point evaluated. The number of viable ***chondrocytes*** in non-transfected and transfected spheres increased over the period of cultivation. In vivo, luciferase activity was maximal at day 5 post-transfection, declined by day 16, but was still present at day 32. On histological analysis, the alginate-chondrocyre spheres filled the cartilage defects and were surrounded by a fibrous repair tissue composed of spindle-shaped cells. Conclusions: These data demonstrate the successful introduction of articular chondrocytes modified by lipid-mediated gene transfer in a ***gel*** suspension delivery system into osteochondral defects and the sustained expression of the transgene in vivo. This method may be used to define the effects of genes involved in cartilage repair and may provide alternative treatments for articular cartilage defects. Copyright .COPYRGT. 2003 John Wiley & Sons, Ltd.

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AN 2002189937 EMBASE
TI A Kruppel-associated box-zinc finger protein, NT2, represses cell-type-specific promoter activity of the .alpha.2(XI) collagen gene.
AU Tanaka K.; Tsumaki N.; Kozak C.A.; Matsumoto Y.; Nakatani F.; Iwamoto Y.; Yamada Y.
CS Y. Yamada, Building 30, NIDCR, NIH, Bethesda, MD 20892, United States. yoshi.yamada@nih.gov
SO Molecular and Cellular Biology, (2002) Vol. 22, No. 12, pp. 4256-4267. .
Refs: 60
ISSN: 0270-7306 CODEN: MCEBD4
CY United States
DT Journal; Article
FS 029 Clinical Biochemistry
LA English
SL English
ED Entered STN: 27 Jun 2002
Last Updated on STN: 27 Jun 2002
AB Type XI collagen is composed of three chains, .alpha.1(XI), .alpha.2(XI), and .alpha.3(XI), and plays a critical role in the formation of cartilage collagen fibrils and in skeletal morphogenesis. It was previously reported that the -530-bp promoter segment of the .alpha.2(XI) collagen gene (Col11a2) was sufficient for cartilage-specific expression and that a 24-bp sequence from this segment was able to switch promoter activity from neural tissues to cartilage in transgenic mice when this sequence was placed in the heterologous neurofilament light gene (NFL) promoter. To identify a protein factor that bound to the 24-bp sequence of the Col11a2 promoter, we screened a mouse limb bud cDNA expression library in the yeast one-hybrid screening system and obtained the cDNA clone NT2. Sequence analysis revealed that NT2 is a zinc finger protein consisting of a Kruppel-associated box (KRAB) and is a homologue of human FPM315, which was previously isolated by random cloning and sequencing. The KRAB domain has been found in a number of zinc finger proteins and implicated as a transcriptional repression domain, although few target genes for KRAB-containing zinc finger proteins has been identified. Here, we demonstrate that NT2 functions as a negative regulator of Col11a2. In situ hybridization analysis of developing mouse cartilage showed that NT2 mRNA is highly expressed by hypertrophic ***chondrocytes*** but is minimally expressed by resting and proliferating ***chondrocytes*** , in an inverse correlation with the expression patterns of Col11a2. ***Gel*** shift assays showed that NT2 bound a specific sequence within the 24-bp site of the Col11a2 promoter. We found that Col11a2 promoter activity was inhibited by transfection of the NT2 expression ***vector*** in RSC cells, a chondrosarcoma cell line. The expression ***vector*** for mutant NT2 lacking the KRAB domain failed to inhibit Col11a2 promoter activity. These results demonstrate that KRAB- zinc finger protein NT2 inhibits transcription of its physiological target gene, suggesting a novel regulatory mechanism of cartilage-specific expression of Col11a2.

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AN 2003453915 EMBASE
TI The Transcription Factor SOX9 Regulates Cell Cycle and Differentiation Genes in Chondrocytic CFK2 Cells.
AU Panda D.K.; Miao D.; Lefebvre V.; Hendy G.N.; Goltzman D.
CS D. Goltzman, Calcium Research Laboratory, Royal Victoria Hospital, 687 Pine Ave. W., Montreal, Que. H3A 1A1, Canada. david.goltzman@mcgill.ca
SO Journal of Biological Chemistry, (2 Nov 2001) Vol. 276, No. 44, pp. 41229-41236. .
Refs: 51
ISSN: 0021-9258 CODEN: JBCHA3
CY United States
DT Journal; Article
FS 029 Clinical Biochemistry
LA English
SL English
ED Entered STN: 4 Dec 2003
Last Updated on STN: 4 Dec 2003
AB SOX9 is a transcription factor that is essential for ***chondrocyte*** differentiation and cartilage formation. We stably overexpressed SOX9 cDNA in the rat chondrocytic cell line CFK2. Compared with the ***vector*** control, a greater proportion of SOX9-transfected cells accumulated in the G (0)/G(1) phase. This was associated with an increase in mRNA and protein expression of p21(cip1), an inhibitor of cyclin-dependent kinase activity. SOX9 enhanced p21(cip1) promoter activity in a luciferase reporter assay. CFK2 cells overexpressing SOX9 became more elongated and adhesive and demonstrated a shift in cytoplasmic F-actin distribution. N-cadherin mRNA levels were elevated in the SOX9-transfected cells, and SOX9 enhanced N-cadherin promoter activity. By electrophoretic mobility shift assay, nuclear extracts of SOX9-transfected CFK2 cells specifically bound an oligonucleotide comprising an N-cadherin promoter region containing a consensus SOX9-binding motif. The transcriptional activity of SOX9 depended upon nuclear localization signals required for SOX9 nuclear entry. Differentiation of transfected CFK2 cells was accelerated as evidenced by more rapid accumulation of alkaline phosphatase activity, increased production of proteoglycans, and increased calcium accumulation, and this was associated with decreased ERK1 expression. These studies demonstrate that SOX9 alters the rate of cell cycle progression of chondrocytes and their differentiation by enhancing or inhibiting the expression of selected genes, including p21(cip1) and ERK1, and that N-cadherin is an additional direct target of this transcriptional regulator.

L9 ANSWER 11 OF 11 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN DUPLICATE 6
AN 2000211169 EMBASE
TI Ex vivo gene delivery using an adenovirus vector in treatment for cartilage defects.
AU Ikeda T.; Kubo T.; Nakanishi T.; Arai Y.; Kobayashi K.; Mazda O.; Ohashi S.; Takahashi K.; Imanishi J.; Takigawa M.; Hirasawa Y.
CS Dr. T. Kubo, Department of Orthopaedic Surgery, Kyoto Prefectural Univ. of Medicine, Kajiicho 465, Kawaramachi-Hirokoji, Kyoto 602-8566, Japan
SO Journal of Rheumatology, (2000) Vol. 27, No. 4, pp. 990-996. .
Refs: 34
ISSN: 0315-162X CODEN: JRHUA
CY Canada
DT Journal; Article
FS 004 Microbiology
031 Arthritis and Rheumatism
LA English
SL English
ED Entered STN: 6 Jul 2000
Last Updated on STN: 6 Jul 2000
AB Objective. To realize local selective gene expression in grafted ***chondrocytes*** for cartilage defect, we investigated the usefulness of an ex vivo gene delivery method using an adenovirus ***vector*** . Methods. .beta.- galactosidase gene (LacZ) was transfected using an adenovirus ***vector*** to ***chondrocytes*** isolated from rat joints. The cells were then embedded into collagen ***gel*** , and LacZ expression in the ***gel*** was examined using 5-bromo-4-chloro-3-indolyl-.beta.-D-galactopyranoside (X-gal) staining; .beta.-galactosidase activity was also measured. The collagen ***gel*** containing transfected ***chondrocytes*** was grafted to the experimental cartilage defects, and the expression of delivered gene was histologically examined after X-gal staining of the tissue containing the grafted area. Results. X-gal positive chondrocytes in the ***gel*** accounted for 82% at one week and 55% at 8 weeks after gene delivery. .beta.-galactosidase activity decreased with time, but its expression was maintained even at 8 weeks after gene delivery. Chondrocytes used in the allograft maintained their morphology, and the expression of delivered gene continued during the 8 week period. Conclusion. In this ex vivo method, delivered gene can be expressed efficiently for a long time; this method would be useful in allografts for cartilage defects.

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☐	L5	L4 same (disease or disorder)	545
☐	L4	L1 same (brain or heart or liver or kidney or GI tract or spleen or smooth muscle or skeletal muscle or eye or ganglion or lung or gonads or pancreas)	2990
☐	L3	L1 near3 vector	21
☐	L2	L1 near vector	3
☐	L1	chondrocyte	10389

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